Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	21	dinman.in. or peltz-stuart.in.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/08/21 11:01
L2	69	ribosomal adj frameshift	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/08/21 11:02
L3	0	l2 with increase near frequency	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/08/21 11:02
L4	0	l2 with (increase near5 frequency)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/08/21 11:02
L5	0	l2 with (increase with frequency)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/08/21 11:02
L6	6	l1 and l2	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/08/21 11:02

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     (FILE 'HOME' ENTERED AT 10:37:43 ON 21 AUG 2005)

     FILE 'MEDLINE, BIOSIS, CAPLUS, SCISEARCH' ENTERED AT 10:37:56 ON 21 AUG
     2005
L1          7623 S FRAMESHIFT AND DISEASE
L2        268492 S INCREASE AND FREQUENCY
L3            70 S L1 AND L2
L4            49 DUP REMOVE L3 (21 DUPLICATES REMOVED)
                 E DINMAN/AU
L5            93 S E10 OR E11 OR E12
L6            40 S L5 AND RIBOSOMAL AND FRAMESHIFT
L7            26 DUP REMOVE L6 (14 DUPLICATES REMOVED)
                 E PELTZ/AU
                 E PELTZ S
                 E PELTZ STUART/AU
L8           159 S E3 OR E4
L9             0 S L8 AND RIBOSOMAL FRAMESHIFT AND TREATMENT
L10            2 S L8 AND RIBOSOMAL FRAMESHIFT AND DISEASE
L11           10 S L8 AND RIBOSOMAL FRAMESHIFT
L12            6 DUP REMOVE L11 (4 DUPLICATES REMOVED)

=>
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L4 ANSWER 3 OF 49 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004290841 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15122511
TITLE: CHEK2*1100delC and susceptibility to breast cancer: a collaborative analysis involving 10,860 breast cancer cases and 9,065 controls from 10 studies.
AUTHOR: Anonymous
CORPORATE SOURCE: CHEK2 Breast Cancer Case-Control Consortium.
SOURCE: American journal of human genetics, (2004 Jun) 74 (6) 1175-82. Electronic Publication: 2004-04-30. Journal code: 0370475. ISSN: 0002-9297.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040615
Last Updated on STN: 20040707
Entered Medline: 20040706

AB Previous studies of families with multiple cases of breast cancer have indicated that a **frameshift** alteration in the CHEK2 gene, 1100delC, is associated with an elevated **frequency** of breast cancer in such families, but the risk associated with the variant in other situations is uncertain. To evaluate the breast cancer risk associated with this variant, 10,860 breast cancer cases and 9,065 controls from 10 case-control studies in five countries were genotyped. CHEK2*1100delC was found in 201 cases (1.9%) and 64 controls (0.7%) (estimated odds ratio 2.34; 95% CI 1.72-3.20; P=.0000001). There was some evidence of a higher prevalence of CHEK2*1100delC among cases with a first-degree relative affected with breast cancer (odds ratio 1.44; 95% CI 0.93-2.23; P=.10) and of a trend for a higher breast cancer odds ratio at younger ages at diagnosis (P=.002). These results confirm that CHEK2*1100delC confers an increased risk of breast cancer and that this risk is apparent in women unselected for family history. The results are consistent with the hypothesis that CHEK2*1100delC multiplies the risks associated with susceptibility alleles in other genes to **increase** the risk of breast cancer.

L7 ANSWER 1 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:448045 SCISEARCH
THE GENUINE ARTICLE: 916PR
TITLE: Torsional restraint: a new twist on frameshifting pseudoknots
AUTHOR: Plant E P; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Cell Biol & Mol Genet, Microbiol Bldg Room 2135, College Pk, MD 20742 USA (Reprint); Univ Maryland, Dept Cell Biol & Mol Genet, College Pk, MD 20742 USA
dinman@umd.edu
COUNTRY OF AUTHOR: USA
SOURCE: NUCLEIC ACIDS RESEARCH, (2005) Vol. 33, No. 6, pp. 1825-1833.
ISSN: 0305-1048.
PUBLISHER: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 30
ENTRY DATE: Entered STN: 5 May 2005
Last Updated on STN: 5 May 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB mRNA pseudoknots have a stimulatory function in programmed -1 **ribosomal** frameshifting (-1 PRF). Though we previously presented a model for how mRNA pseudoknots might activate the mechanism for -1 PRF, it did not address the question of the role that they may play in positioning the mRNA relative to the ribosome in this process [E. P. Plant, K. L. M. Jacobs, J. W. Harger, A. Meskauskas, J. L. Jacobs, J. L. Baxter, A. N. Petrov and J. D. Dinman (2003) RNA, 9, 168-174]. A separate 'torsional restraint' model suggests that mRNA pseudoknots act to increase the fraction of ribosomes directed to pause with the upstream heptameric slippery site positioned at the ribosome's A- and P-decoding sites [J. D. Dinman (1995) Yeast, 11, 1115-1127]. Here, experiments using a series of 'pseudo-pseudoknots' having different degrees of rotational freedom were used to test this model. The results of this study support the mechanistic hypothesis that -1 **ribosomal** frameshifting is enhanced by torsional resistance of the mRNA pseudoknot.

L7 ANSWER 2 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:675174 SCISEARCH
THE GENUINE ARTICLE: 938IK
TITLE: A three-stemmed mRNA pseudoknot in the SARS coronavirus **frameshift** signal
AUTHOR: Plant E P; Perez-Alvarado G C; Jacobs J L; Mukhopadhyay B; Hennig M; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Mol Genet & Cell Biol, College Pk, MD 20742 USA (Reprint); Scripps Res Inst, Dept Mol Biol, La Jolla, CA 92037 USA; Scripps Res Inst, Skaggs Inst Chem Biol, La Jolla, CA 92037 USA
dinman@umd.edu
COUNTRY OF AUTHOR: USA
SOURCE: PLOS BIOLOGY, (JUN 2005) Vol. 3, No. 6, arn. e172.
ISSN: 1544-9173.
PUBLISHER: PUBLIC LIBRARY SCIENCE, 185 BERRY ST, STE 1300, SAN FRANCISCO, CA 94107 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 56
ENTRY DATE: Entered STN: 8 Jul 2005
Last Updated on STN: 22 Jul 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A wide range of RNA viruses use programmed -1 **ribosomal** frameshifting for the production of viral fusion proteins. Inspection of the overlap regions between ORF1a and ORF1b of the SARS-CoV genome revealed that, similar to all coronaviruses, a programmed -1

ribosomal frameshift could be used by the virus to produce a fusion protein. Computational analyses of the **frameshift** signal predicted the presence of an mRNA pseudoknot containing three double-stranded RNA stem structures rather than two. Phylogenetic analyses showed the conservation of potential three-stemmed pseudoknots in the **frameshift** signals of all other coronaviruses in the GenBank database. Though the presence of the three-stemmed structure is supported by nuclease mapping and two-dimensional nuclear magnetic resonance studies, our findings suggest that interactions between the stem structures may result in local distortions in the A-form RNA. These distortions are particularly evident in the vicinity of predicted A-bulges in stems 2 and 3. In vitro and in vivo frameshifting assays showed that the SARS-CoV **frameshift** signal is functionally similar to other viral **frameshift** signals: it promotes efficient frameshifting in all of the standard assay systems, and it is sensitive to a drug and a genetic mutation that are known to affect frameshifting efficiency of a yeast virus. Mutagenesis studies reveal that both the specific sequences and structures of stems 2 and 3 are important for efficient frameshifting. We have identified a new RNA structural motif that is capable of promoting efficient programmed **ribosomal** frameshifting. The high degree of conservation of three- stemmed mRNA pseudoknot structures among the coronaviruses suggests that this presents a novel target for antiviral therapeutics.

L7 ANSWER 3 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:201322 SCISEARCH
THE GENUINE ARTICLE: 774NH
TITLE: A programmed-1 **ribosomal frameshift** signal can function as a cis-acting mRNA destabilizing element
AUTHOR: Plant E P; Wang P G; Jacobs J L; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Mol Genet & Cell Biol, Microbiol Bldg Room 2135, College Pk, MD 20742 USA (Reprint); Univ Maryland, Dept Mol Genet & Cell Biol, College Pk, MD 20742 USA; Centocor Inc, Pharmaceut Sci, Raritan, NJ 08869 USA
COUNTRY OF AUTHOR: USA
SOURCE: NUCLEIC ACIDS RESEARCH, (JAN 2004) Vol. 32, No. 2, pp. 784-790.
ISSN: 0305-1048.
PUBLISHER: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34
ENTRY DATE: Entered STN: 5 Mar 2004
Last Updated on STN: 5 Mar 2004

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Nonsense-mediated mRNA decay (NMD) directs rapid degradation of premature termination codon (PTC)-containing mRNAs, e.g. those containing **frameshift** mutations. Many viral mRNAs encode polycistronic messages where programmed -1 **ribosomal frameshift** (-1 PRF) signals direct ribosomes to synthesize polyproteins. A previous study, which identified consensus -1 PRF signals in the yeast genome, found that, in contrast to viruses, the majority of predicted -1 PRF events would direct translating ribosomes to PTCs. Here we tested the hypothesis that a -1 PRF signal can function as a cis-acting mRNA destabilizing element by inserting an L-A viral -1 PRF signal into a PGK1 reporter construct in the 'genomic' orientation. The results show that even low levels of -1 PRF are sufficient to target the reporter mRNA for degradation via the NMD pathway, with half-lives similar to messages containing in-frame PTCs. The demonstration of an inverse correlation between **frameshift** efficiency and mRNA half-lives suggests that modulation of -1 PRF frequencies can be used to post-transcriptionally regulate gene expression. Analysis of the mRNA decay profiles of the **frameshift**-signal- containing reporter mRNAs also supports the notion that NMD remains active on mRNAs beyond the 'pioneer round' of translation in yeast.

L7 ANSWER 4 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:1050719 SCISEARCH
THE GENUINE ARTICLE: 874PK
TITLE: Systematic analysis of bicistronic reporter assay data
AUTHOR: Jacobs J L; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Cell Biol & Mol Genet, 2135 Microbiol Bldg, College Pk, MD 20742 USA (Reprint); Univ Maryland, Dept Cell Biol & Mol Genet, College Pk, MD 20742 USA dinman@umd.edu
COUNTRY OF AUTHOR: USA
SOURCE: NUCLEIC ACIDS RESEARCH, (2004) Vol. 32, No. 20, arn. e160. ISSN: 0305-1048.
PUBLISHER: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 32
ENTRY DATE: Entered STN: 27 Dec 2004
Last Updated on STN: 27 Dec 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Bicistronic reporter assay systems have become a mainstay of molecular biology. While the assays themselves encompass a broad range of diverse and unrelated experimental protocols, the numerical data garnered from these experiments often have similar statistical properties. In general, a primary dataset measures the paired expression of two internally controlled reporter genes. The expression ratio of these two genes is then normalized to an external control reporter. The end result is a 'ratio of ratios' that is inherently sensitive to propagation of the error contributed by each of the respective numerical components. The statistical analysis of this data therefore requires careful handling in order to control for the propagation of error and its potentially misleading effects. A careful survey of the literature found no consistent method for the statistical analysis of data generated from these important and informative assay systems. In this report, we present a detailed statistical framework for the systematic analysis of data obtained from bicistronic reporter assay systems. Specifically, a dual luciferase reporter assay was employed to measure the efficiency of four programmed -1 **frameshift** signals. These **frameshift** signals originate from the L-A virus, the SARS-associated Coronavirus and computationally identified **frameshift** signals from two Saccharomyces cerevisiae genes. Furthermore, these statistical methods were applied to prove that the effects of anisomycin on programmed -1 frameshifting are statistically significant. A set of Microsoft Excel spreadsheets, which can be used as templates for data generated by dual reporter assay systems, and an online tutorial are available at our website (http://dinmanlab.umd.edu/statistics). These spreadsheets could be easily adapted to any bicistronic reporter assay system.

L7 ANSWER 5 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:221442 SCISEARCH
THE GENUINE ARTICLE: 651AJ
TITLE: Delayed rRNA processing results in significant ribosome biogenesis and functional defects
AUTHOR: Meskauskas A; Baxter J L; Carr E A; Yasenchak J; Gallagher J E G; Baserga S J; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Mol Genet & Cell Biol, College Pk, MD 20742 USA (Reprint); Rutgers State Univ, Grad Sch Biomed Sci, Piscataway, NJ 08854 USA; Univ Med & Dent New Jersey, Robert Wood Johnson Med Sch, Piscataway, NJ 08854 USA; Yale Univ, Sch Med, Dept Mol Biophys & Biochem, New Haven, CT 06520 USA
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (MAR 2003) Vol. 23, No. 5, pp. 1602-1613.
ISSN: 0270-7306.
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC

20036-2904 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 82
ENTRY DATE: Entered STN: 21 Mar 2003
Last Updated on STN: 21 Mar 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB mof6-1 was originally isolated as a recessive mutation in Saccharomyces cerevisiae which promoted increased efficiencies of programmed -1 **ribosomal** frameshifting and rendered cells unable to maintain the killer virus. Here, we demonstrate that mof6-1 is a unique allele of the histone deacetylase RPD3, that the deacetylase function of Rpd3p is required for controlling wild-type levels of frameshifting and virus maintenance, and that the closest human homolog can fully complement these defects. Loss of the Rpd3p-associated histone deacetylase function, either by mutants of rpd3 or loss of the associated gene product Sin3p or Sap30p, results in a delay in rRNA processing rather than in an rRNA transcriptional defect. This results in production of ribosomes having lower affinities for aminoacyl-tRNA and diminished peptidyltransferase activities. We hypothesize that decreased rates of peptidyl transfer allow ribosomes with both A and P sites occupied by tRNAs to pause for longer periods of time at -1 **frameshift** signals, promoting increased programmed -1 **ribosomal** frameshifting efficiencies and subsequent loss of the killer virus. The frameshifting defect is accentuated when the demand for ribosomes is highest, suggesting that rRNA posttranscriptional modification is the bottleneck in ribosome biogenesis.

L7 ANSWER 6 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:663539 SCISEARCH
THE GENUINE ARTICLE: 705DZ
TITLE: Decreased peptidyltransferase activity correlates with increased programmed-1 **ribosomal** frameshifting and viral maintenance defects in the yeast Saccharomyces cerevisiae
AUTHOR: Meskauskas A; Harger J W; Jacobs K L M; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Mol Genet & Cell Biol, Microbiol Bldg, Room 2135, College Pk, MD 20742 USA (Reprint); Univ Maryland, Dept Mol Genet & Cell Biol, College Pk, MD 20742 USA; Rutgers State Univ, Univ Med & Dent New Jersey, Program Mol Biosci, Piscataway, NJ 08854 USA
COUNTRY OF AUTHOR: USA
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (AUG 2003) Vol. 9, No. 8, pp. 982-992.
ISSN: 1355-8382.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 68
ENTRY DATE: Entered STN: 15 Aug 2003
Last Updated on STN: 15 Aug 2003
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB increased efficiencies of programmed -1 **ribosomal** frameshifting in yeast cells expressing mutant forms of **ribosomal** protein L3 are unable to maintain the dsRNA "Killer" virus. Here we demonstrate that changes in frameshifting and virus maintenance in these mutants correlates with decreased peptidlyltransferase activities. The mutants did not affect Ty1-directed programmed +1 **ribosomal** frameshifting or nonsense-mediated mRNA decay. independent experiments demonstrate similar programmed -1 **ribosomal** frameshifting specific defects in cells lacking **ribosomal** protein L41, which has previously been shown to result in peptidyltransferase defects in yeast. These findings are consistent with the hypothesis that decreased peptidyltransferase activity should result in longer ribosome pause times after the accommodation step of the elongation cycle, allowing more time for **ribosomal** slippage at programmed -1 **ribosomal**

frameshift signals.

L7 ANSWER 7 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:224757 SCISEARCH
THE GENUINE ARTICLE: 650UK
TITLE: The 9-angstrom solution: How mRNA pseudoknots promote efficient programmed -1 **ribosomal** frameshifting
AUTHOR: Plant E P; Jacobs K L M; Harger J W; Meskauskas A; Jacobs J L; Baxter J L; Petrov A N; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Cell Biol & Mol Genet, Microbiol Bldg, Rm 2135, College Pk, MD 20742 USA (Reprint); Univ Maryland, Dept Cell Biol & Mol Genet, College Pk, MD 20742 USA; Rutgers Univ Med & Dent New Jersey, Dept Microbiol & Mol Genet, Robert Wood Johnson Med Sch, Piscataway, NJ 08854 USA; Rutgers Univ Med & Dent New Jersey, Grad Programs Mol Biosci, Robert Wood Johnson Med Sch, Piscataway, NJ 08854 USA
COUNTRY OF AUTHOR: USA
SOURCE: RNA-A PUBLICATION OF THE RNA SOCIETY, (FEB 2003) Vol. 9, No. 2, pp. 168-174.
ISSN: 1355-8382.
PUBLISHER: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA.
DOCUMENT TYPE: Editorial; Journal
LANGUAGE: English
REFERENCE COUNT: 60
ENTRY DATE: Entered STN: 21 Mar 2003
Last Updated on STN: 21 Mar 2003

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB There is something special about mRNA pseudoknots that allows them to elicit efficient levels of programmed -1 **ribosomal** frameshifting. Here, we present a synthesis of recent crystallographic, molecular, biochemical, and genetic studies to explain this property. Movement of 9 A by the anticodon loop of the aminoacyl-tRNA at the accommodation step normally pulls the downstream mRNA a similar distance along with it. We suggest that the downstream mRNA pseudoknot provides resistance to this movement by becoming wedged into the entrance of the **ribosomal** mRNA tunnel. These two opposing forces result in the creation of a local region of tension in the mRNA between the A-site codon and the mRNA pseudoknot. This can be relieved by one of two mechanisms; unwinding the pseudoknot, allowing the downstream region to move forward, or by slippage of the proximal region of the mRNA backwards by one base. The observed result of the latter mechanism is a net shift of reading frame by one base in the 5' direction, that is, a -1 **ribosomal** **frameshift**.

L7 ANSWER 8 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:367291 SCISEARCH
THE GENUINE ARTICLE: 543DX
TITLE: The **frameshift** signal of HIV-1 involves a potential intramolecular triplex RNA structure
AUTHOR: **Dinman J D (Reprint)**; Richter S; Plant E P; Taylor R C; Hammell A B; Rana T M
CORPORATE SOURCE: Univ Maryland, Dept Cell Biol & Mol Genet, 2135 Microbiol Bldg, College Pk, MD 20742 USA (Reprint); Univ Maryland, Dept Cell Biol & Mol Genet, College Pk, MD 20742 USA; Univ Massachusetts, Sch Med, Chem Biol Program, Dept Biochem & Mol Pharmacol, Worcester, MA 01605 USA; Univ Med & Dent New Jersey, Robert Wood Johnson Med Sch, Dept Mol Genet & Microbiol, Piscataway, NJ 08854 USA; Univ Colorado, Hlth Sci Ctr, Dept Pharmacol, Denver, CO 80262 USA
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (16 APR 2002) Vol. 99, No. 8, pp. 5331-5336.
ISSN: 0027-8424.
PUBLISHER: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON,

DC 20418 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 54
ENTRY DATE: Entered STN: 10 May 2002
Last Updated on STN: 10 May 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The cis-acting mRNA elements that promote programmed -1 **ribosomal** frameshifting present a natural target for the rational design of antiretroviral chemotherapies. It has been commonly accepted that the HIV-1 frameshifting signal is special, because its downstream enhancer element consists of a simple mRNA stem loop rather than a more complex secondary structure such as a pseudoknot. Here we present three lines of evidence, bioinformatic, structural, and genetic, showing that the biologically relevant HIV-1 **frameshift** signal contains a complex RNA structure that likely includes an extended RNA triple-helix region. We suggest that the potential intramolecular triplex structure is essential for viral propagation and viability, and that small molecules targeted to this RNA structure may possess antiretroviral activities.

L7 ANSWER 9 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:768773 SCISEARCH
THE GENUINE ARTICLE: 593HZ
TITLE: An 'integrated model' of programmed **ribosomal** frameshifting
AUTHOR: Harger J W (Reprint); Meskauskas A; **Dinman J D**
CORPORATE SOURCE: Rutgers State Univ, Grad Sch Biomed Sci, Piscataway, NJ 08854 USA (Reprint); Univ Med & Dent New Jersey, Robert Wood Johnson Med Sch, Dept Mol Genet & Microbiol, Piscataway, NJ 08854 USA; Univ Maryland, Dept Cell Biol & Mol Genet, College Pk, MD 20742 USA
COUNTRY OF AUTHOR: USA
SOURCE: TRENDS IN BIOCHEMICAL SCIENCES, (SEP 2002) Vol. 27, No. 9, pp. 448-454.
ISSN: 0968-0004.
PUBLISHER: ELSEVIER SCIENCE LONDON, 84 THEOBALDS RD, LONDON WC1X 8RR, ENGLAND.
DOCUMENT TYPE: Editorial; Journal
LANGUAGE: English
REFERENCE COUNT: 49
ENTRY DATE: Entered STN: 4 Oct 2002
Last Updated on STN: 4 Oct 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Many viral mRNAs, including those of HIV-1, can make translating ribosomes change reading frame. Altering the efficiencies of programmed **ribosomal frameshift** (PRF) inhibits viral propagation. As a new target for potential antiviral agents, it is therefore important to understand how PRF is controlled Incorporation of the current models describing PRF into the context of the translation elongation cycle leads us to propose an 'integrated model' of PRF both as a guide towards further characterization of PRF at the molecular and biochemical levels, and for the identification of new targets for antiviral therapeutics.

L7 ANSWER 10 OF 26 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:752201 SCISEARCH
THE GENUINE ARTICLE: 589UL
TITLE: New targets for antivirals: The **ribosomal** A-site and the factors that interact with it
AUTHOR: Kinzy T G; Harger J W; Carr-Schmid A; Kwon J; Shastry M; Justice M; **Dinman J D (Reprint)**
CORPORATE SOURCE: Univ Maryland, Dept Mol Genet & Cell Biol, College Pk, MD 20742 USA (Reprint); Canc Inst New Jersey, Piscataway, NJ 08854 USA; Dept Human & Anim Infect Dis Res, Merck Res Labs, Rahway, NJ 08065 USA; Univ Med & Dent New Jersey, Robert Wood Johnson Med Sch, Grad Program Mol Biosci UMDNJ Rutgers Univ, Piscataway, NJ 08854 USA; Univ Med & Dent New Jersey, Robert Wood Johnson Med Sch, Dept Mol Genet &

Microbiol, Piscataway, NJ 08854 USA
COUNTRY OF AUTHOR: USA
SOURCE: VIROLOGY, (15 AUG 2002) Vol. 300, No. 1, pp. 60-70. ISSN: 0042-6822.
PUBLISHER: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36
ENTRY DATE: Entered STN: 27 Sep 2002
Last Updated on STN: 27 Sep 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Many viruses use programmed -1 **ribosomal** frameshifting to ensure the correct ratio of viral structural to enzymatic proteins. Alteration of **frameshift** efficiencies changes these ratios, in turn inhibiting viral particle assembly and virus propagation, Previous studies determined that anisomycin, a peptidyl transferase inhibitor, specifically inhibited -1 frameshifting and the ability of yeast cells to propagate the L-A and M, dsRNA viruses (J. D. Dinman, M. J. Ruiz-Echevarria, K. Czaplinski, and S. W. Peitz, 1997, Proc. Natl. Acad. Sci. USA 94, 6606-6611). Here we show that preussin, a pyrollidine that is structurally similar to anisomycin (R. E. Schwartz, J. Liesch, O. Hensens, L. Zitano, S. Honeycutt, G. Garrity, R. A. Fromtling, J. Onishi, and R. Monaghan, 1988. J. Antibiot. (Tokyo) 41, 1774--1779), also inhibits - 1 programmed **ribosomal** frameshifting and virus propagation by acting at the same site or through the same mechanism as anisomycin. Since anisomycin is known to assert its effect at the **ribosomal** A-site, we undertook a pharmacogenetic analysis of mutants of trans-acting eukaryotic elongation factors (eEFs) that function at this region of the ribosome. Among mutants of eEF1A, a correlation is observed between resistance/susceptibility profiles to preussin and anisomycin, and these in turn correlate with programmed -1 **ribosomal** frameshifting efficiencies and killer virus phenotypes. Among mutants of eEF2, the extent of resistance to preussin correlates with resistance to sordarin, an eEF2 inhibitor. These results suggest that structural features associated with the **ribosomal** A-site and with the trans-acting factors that interact with it may present a new set of molecular targets for the rational design of antiviral compounds. (C) 2002 Elsevier Science (USA).

L7 ANSWER 11 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2001667749 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11713264
TITLE: Saturation mutagenesis of 5S rRNA in Saccharomyces cerevisiae.
AUTHOR: Smith M W; Meskauskas A; Wang P; Sergiev P V; **Dinman J D**
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Rutgers University and University of Medicine and Dentistry of New Jersey, 675 Hoes Lane, Piscataway, NJ 08854, USA.
CONTRACT NUMBER: R01 GM58859 (NIGMS)
R01 GM62143 (NIGMS)
SOURCE: Molecular and cellular biology, (2001 Dec) 21 (24) 8264-75. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011120
Last Updated on STN: 20020123
Entered Medline: 20011221

AB rRNAs are the central players in the reactions catalyzed by ribosomes, and the individual rRNAs are actively involved in different ribosome functions. Our previous demonstration that yeast 5S rRNA mutants (called mof9) can impact translational reading frame maintenance showed an unexpected function for this ubiquitous biomolecule. At the time, however, the highly repetitive nature of the genes encoding rRNAs precluded more detailed genetic and molecular analyses. A new genetic

system allows all 5S rRNAs in the cell to be transcribed from a small, easily manipulated plasmid. The system is also amenable for the study of the other rRNAs, and provides an ideal genetic platform for detailed structural and functional studies. Saturation mutagenesis reveals regions of 5S rRNA that are required for cell viability, translational accuracy, and virus propagation. Unexpectedly, very few lethal alleles were identified, demonstrating the resilience of this molecule. Superimposition of genetic phenotypes on a physical map of 5S rRNA reveals the existence of phenotypic clusters of mutants, suggesting that specific regions of 5S rRNA are important for specific functions. Mapping these mutants onto the Haloarcula marismortui large subunit reveals that these clusters occur at important points of physical interaction between 5S rRNA and the different functional centers of the ribosome. Our analyses lead us to propose that one of the major functions of 5S rRNA may be to enhance translational fidelity by acting as a physical transducer of information between all of the different functional centers of the ribosome.

L7 ANSWER 12 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2001451933 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11497428
TITLE: **Ribosomal** protein L5 helps anchor peptidyl-tRNA to the P-site in Saccharomyces cerevisiae.
AUTHOR: Meskauskas A; **Dinman J D**
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, Piscataway 08854, USA.
CONTRACT NUMBER: R01 GM58859 (NIGMS)
R01 GM62143 (NIGMS)
SOURCE: RNA (New York, N.Y.), (2001 Aug) 7 (8) 1084-96.
Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010903
Entered Medline: 20010830
AB Our previous demonstration that mutants of 5S rRNA called mof9 can specifically alter efficiencies of programmed **ribosomal** frameshifting (PRF) suggested a role for this ubiquitous molecule in the maintenance of translational reading frame, though the repetitive nature of the 5S rDNA gene (>100 copies/cell) inhibited more detailed analyses. However, given the known interactions between 5S rRNA and **ribosomal** protein L5 (previously called L1 or YL3) encoded by an essential, single-copy gene, we monitored the effects of a series of well-defined rpl5 mutants on PRF and virus propagation. Consistent with the mof9 results, we find that the rpl5 mutants promoted increased frameshifting efficiencies in both the -1 and +1 directions, and conferred defects in the ability of cells to propagate two endogenous viruses. Biochemical analyses demonstrated that mutant ribosomes had decreased affinities for peptidyl-tRNA. Pharmacological studies showed that sparsomycin, a peptidyltransferase inhibitor that specifically increases the binding of peptidyl-tRNA with ribosomes, was antagonistic to the frameshifting defects of the most severe mutant, and the extent of sparsomycin resistance correlated with the severity of the frameshifting defects in all of the mutants. These results provide biochemical and physiological evidence that one function of L5 is to anchor peptidyl-tRNA to the P-site. A model is presented describing how decreased affinity of ribosomes for peptidyl-tRNA can affect both -1 and +1 frameshifting, and for the effects of sparsomycin.

L7 ANSWER 13 OF 26 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2000115854 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10648594
TITLE: Kinetics of **ribosomal** pausing during programmed -1 translational frameshifting.
AUTHOR: Lopinski J D; **Dinman J D**; Bruenn J A
CORPORATE SOURCE: Department of Biological Sciences, State University of New

York at Buffalo, Buffalo, New York 14260, USA.
CONTRACT NUMBER: GM22200 (NIGMS)
GM58859 (NIGMS)
SOURCE: Molecular and cellular biology, (2000 Feb) 20 (4) 1095-103.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000215

AB In the Saccharomyces cerevisiae double-stranded RNA virus, programmed -1 **ribosomal** frameshifting is responsible for translation of the second open reading frame of the essential viral RNA. A typical slippery site and downstream pseudoknot are necessary for this frameshifting event, and previous work has demonstrated that ribosomes pause over the slippery site. The translational intermediate associated with a ribosome paused at this position is detected, and, using in vitro translation and quantitative heelprinting, the rates of synthesis, the **ribosomal** pause time, the proportion of ribosomes paused at the slippery site, and the fraction of paused ribosomes that **frameshift** are estimated. About 10% of ribosomes pause at the slippery site in vitro, and some 60% of these continue in the -1 frame. Ribosomes that continue in the -1 frame pause about 10 times longer than it takes to complete a peptide bond in vitro. Altering the rate of translational initiation alters the rate of frameshifting in vivo. Our in vitro and in vivo experiments can best be interpreted to mean that there are three methods by which ribosomes pass the **frameshift** site, only one of which results in frameshifting.

L7 ANSWER 14 OF 26 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999263228 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10330121
TITLE: Identification of putative programmed -1 **ribosomal** **frameshift** signals in large DNA databases.
COMMENT: Comment in: Genome Res. 1999 May;9(5):393-4. PubMed ID: 10330118
AUTHOR: Hammell A B; Taylor R C; Peltz S W; **Dinman J D**
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, University of Medicine and Dentistry of New Jersey (UMDNJ), Robert Wood Johnson Medical School, and The Graduate Programs in Molecular Bioscience Rutgers/UMDNJ, Piscataway, New Jersey 08854, USA.
CONTRACT NUMBER: R01 GM48631 (NIGMS)
R01 GM58859 (NIGMS)
T32 AI07403-07 (NIAID)
SOURCE: Genome research, (1999 May) 9 (5) 417-27.
Journal code: 9518021. ISSN: 1088-9051.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990712
Last Updated on STN: 19990712
Entered Medline: 19990624

AB The cis-acting elements that promote efficient **ribosomal** frameshifting in the -1 (5') direction have been well characterized in several viral systems. Results from many studies have convincingly demonstrated that the basic molecular mechanisms governing programmed -1 **ribosomal** frameshifting are almost identical from yeast to humans. We are interested in testing the hypothesis that programmed -1 **ribosomal** frameshifting can be used to control cellular gene expression. Toward this end, a computer program was designed to search large DNA databases for consensus -1 **ribosomal** **frameshift** signals. The results demonstrated that consensus programmed -1 **ribosomal** **frameshift** signals can be

identified in a substantial number of chromosomally encoded mRNAs and that they occur with frequencies from two- to sixfold greater than random in all of the databases searched. A preliminary survey of the databases resulting from the computer searches found that consensus **frameshift** signals are present in at least 21 homologous genes from different species, 2 of which are nearly identical, suggesting evolutionary conservation of function. We show that four previously described missense alleles of genes that are linked to human diseases would disrupt putative programmed -1 **ribosomal** **frameshift** signals, suggesting that the **frameshift** signal may be involved in the normal expression of these genes. We also demonstrate that signals found in the yeast RAS1 and the human CCR5 genes were able to promote significant levels of programmed -1 **ribosomal** frameshifting. The significance of these frameshifting signals in controlling gene expression is not known, however.

L7 ANSWER 15 OF 26 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999077976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9858562
TITLE: **Ribosomal** protein L3 mutants alter translational fidelity and promote rapid loss of the yeast killer virus.
AUTHOR: Peltz S W; Hammell A B; Cui Y; Yasenchak J; Puljanowski L; **Dinman J D**
CORPORATE SOURCE: The Cancer Institute of New Jersey, Piscataway, New Jersey 08854, USA.
CONTRACT NUMBER: GM48631 (NIGMS)
T32 AI07403-07 (NIAID)
SOURCE: Molecular and cellular biology, (1999 Jan) 19 (1) 384-91. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990223
Last Updated on STN: 19990223
Entered Medline: 19990210
AB Programmed -1 **ribosomal** frameshifting is utilized by a number of RNA viruses as a means of ensuring the correct ratio of viral structural to enzymatic proteins available for viral particle assembly. Altering frameshifting efficiencies upsets this ratio, interfering with virus propagation. We have previously demonstrated that compounds that alter the kinetics of the peptidyl-transfer reaction affect programmed -1 **ribosomal** **frameshift** efficiencies and interfere with viral propagation in yeast. Here, the use of a genetic approach lends further support to the hypothesis that alterations affecting the ribosome's peptidyltransferase activity lead to changes in frameshifting efficiency and virus loss. Mutations in the RPL3 gene, which encodes a **ribosomal** protein located at the peptidyltransferase center, promote approximately three- to fourfold increases in programmed -1 **ribosomal** **frameshift** efficiencies and loss of the M1 killer virus of yeast. The mak8-1 allele of RPL3 contains two adjacent missense mutations which are predicted to structurally alter the Mak8-1p. Furthermore, a second allele that encodes the N-terminal 100 amino acids of L3 (called L3Delta) exerts a trans-dominant effect on programmed -1 **ribosomal** frameshifting and killer virus maintenance. Taken together, these results support the hypothesis that alterations in the peptidyltransferase center affect programmed -1 **ribosomal** frameshifting.

L7 ANSWER 16 OF 26 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1998337982 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9671745
TITLE: The upf3 protein is a component of the surveillance complex that monitors both translation and mRNA turnover and affects viral propagation.
AUTHOR: Ruiz-Echevarria M J; Yasenchak J M; Han X; **Dinman J D**; Peltz S W
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Robert

Wood Johnson Medical School-University of Medicine and Dentistry of New Jersey, USA.
CONTRACT NUMBER: GM48631 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1998 Jul 21) 95 (15) 8721-6. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980820

AB The nonsense-mediated mRNA decay pathway functions to degrade aberrant mRNAs that contain premature translation termination codons. In Saccharomyces cerevisiae, the Upf1, Upf2, and Upf3 proteins have been identified as trans-acting factors involved in this pathway. Recent results have demonstrated that the Upf proteins may also be involved in maintaining the fidelity of several aspects of the translation process. Certain mutations in the UPF1 gene have been shown to affect the efficiency of translation termination at nonsense codons and/or the process of programmed -1 **ribosomal** frameshifting used by viruses to control their gene expression. Alteration of programmed **frameshift** efficiencies can affect virus assembly leading to reduced viral titers or elimination of the virus. Here we present evidence that the Upf3 protein also functions to regulate programmed -1 **frameshift** efficiency. A upf3-Delta strain demonstrates increased sensitivity to the antibiotic paromomycin and increased programmed -1 **ribosomal frameshift** efficiency resulting in loss of the M1 virus. Based on these observations, we hypothesize that the Upf proteins are part of a surveillance complex that functions to monitor translational fidelity and mRNA turnover.

L7 ANSWER 17 OF 26 MEDLINE on STN
ACCESSION NUMBER: 1998147791 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9488467
TITLE: The Mof2/Sui1 protein is a general monitor of translational accuracy.
AUTHOR: Cui Y; **Dinman J D**; Kinzy T G; Peltz S W
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Robert Wood Johnson Medical School, UMDNJ, Piscataway, New Jersey 08854, USA.
CONTRACT NUMBER: GM48631 (NIGMS)
SOURCE: Molecular and cellular biology, (1998 Mar) 18 (3) 1506-16. Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980326
Last Updated on STN: 20030304
Entered Medline: 19980319

AB Although it is essential for protein synthesis to be highly accurate, a number of cases of directed **ribosomal** frameshifting have been reported in RNA viruses, as well as in procaryotic and eucaryotic genes. Changes in the efficiency of **ribosomal** frameshifting can have major effects on the ability of cells to propagate viruses which use this mechanism. Furthermore, studies of this process can illuminate the mechanisms involved in the maintenance of the normal translation reading frame. The yeast Saccharomyces cerevisiae killer virus system uses programmed -1 **ribosomal** frameshifting to synthesize its gene products. Strains harboring the mof2-1 allele demonstrated a fivefold increase in frameshifting and prevented killer virus propagation. In this report, we present the results of the cloning and characterization of the wild-type MOF2 gene. mof2-1 is a novel allele of SUI1, a gene previously shown to play a role in translation initiation start site selection. Strains harboring the mof2-1 allele demonstrated a mutant start site

selection phenotype and increased efficiency of programmed -1 **ribosomal** frameshifting and conferred paromomycin sensitivity. The increased frameshifting observed in vivo was reproduced in extracts prepared from mof2-1 cells. Addition of purified wild-type Mof2p/Sui1p reduced frameshifting efficiencies to wild-type levels. Expression of the human SUI1 homolog in yeast corrects all of the mof2-1 phenotypes, demonstrating that the function of this protein is conserved throughout evolution. Taken together, these results suggest that Mof2p/Sui1p functions as a general modulator of accuracy at both the initiation and elongation phases of translation.

L7 ANSWER 18 OF 26 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1998105742 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9444997
TITLE: The pokeweed antiviral protein specifically inhibits Ty1-directed +1 **ribosomal** frameshifting and retrotransposition in Saccharomyces cerevisiae.
AUTHOR: Tumer N E; Parikh B A; Li P; **Dinman J D**
CORPORATE SOURCE: Center for Agricultural Molecular Biology, and Department of Plant Pathology, Cook College, Rutgers University, New Brunswick, New Jersey 08903-0231, USA.
SOURCE: Journal of virology, (1998 Feb) 72 (2) 1036-42. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19990129
Entered Medline: 19980218

AB Programmed **ribosomal** frameshifting is a molecular mechanism that is used by many RNA viruses to produce Gag-Pol fusion proteins. The efficiency of these **frameshift** events determines the ratio of viral Gag to Gag-Pol proteins available for viral particle morphogenesis, and changes in **ribosomal frameshift** efficiencies can severely inhibit virus propagation. Since **ribosomal** frameshifting occurs during the elongation phase of protein translation, it is reasonable to hypothesize that agents that affect the different steps in this process may also have an impact on programmed **ribosomal** frameshifting. We examined the molecular mechanisms governing programmed **ribosomal** frameshifting by using two viruses of the yeast Saccharomyces cerevisiae. Here, we present evidence that pokeweed antiviral protein (PAP), a single-chain **ribosomal** inhibitory protein that depurinates an adenine residue in the alpha-sarcin loop of 25S rRNA and inhibits translocation, specifically inhibits Ty1-directed +1 **ribosomal** frameshifting in intact yeast cells and in an in vitro assay system. Using an in vivo assay for Ty1 retrotransposition, we show that PAP specifically inhibits Ty1 retrotransposition, suggesting that Ty1 viral particle morphogenesis is inhibited in infected cells. PAP does not affect programmed -1 **ribosomal frameshift** efficiencies, nor does it have a noticeable impact on the ability of cells to maintain the M1-dependent killer virus phenotype, suggesting that -1 **ribosomal** frameshifting does not occur after the peptidyltransferase reaction. These results provide the first evidence that PAP has viral RNA-specific effects in vivo which may be responsible for the mechanism of its antiviral activity.

L7 ANSWER 19 OF 26 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 97338065 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9192612
TITLE: Peptidyl-transferase inhibitors have antiviral properties by altering programmed -1 **ribosomal** frameshifting efficiencies: development of model systems.
AUTHOR: **Dinman J D**; Ruiz-Echevarria M J; Czaplinski K; Peltz S W
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, University of Medicine and Dentistry of New Jersey, Robert

Wood Johnson Medical School, 675 Hoes Lane, Piscataway, NJ 08854, USA.. dinman@rwja.umdnj.edu
CONTRACT NUMBER: GM48631-01 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997 Jun 24) 94 (13) 6606-11. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19980206
Entered Medline: 19970721
AB The effects of two peptidyl-transferase inhibitors, anisomycin and sparsomycin, on **ribosomal** frameshifting efficiencies and the propagation of yeast double-stranded RNA viruses were examined. At sublethal doses in yeast cells these drugs specifically alter the efficiency of -1, but not of +1, **ribosomal** frameshifting. These compounds promote loss of the yeast L-A double-stranded RNA virus, which uses a programmed -1 **ribosomal frameshift** to produce its Gag-Pol fusion protein. Both of these drugs also change the efficiency of -1 **ribosomal** frameshifting in yeast and mammalian in vitro translation systems, suggesting that they may have applications to control the propagation of viruses of higher eukaryotes, which also use this translational regulatory mechanism. Our results offer a new set of antiviral agents that may potentially have a broad range of applications in the clinical, veterinary, and agricultural fields.

L7 ANSWER 20 OF 26 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 97400129 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9257646
TITLE: Translational misreading: mutations in translation elongation factor 1alpha differentially affect programmed **ribosomal** frameshifting and drug sensitivity.
AUTHOR: **Dinman J D**; Kinzy T G
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School and The Graduate Programs in Molecular Biosciences, Rutgers University and UMDNJ RWJMS, Piscataway, 08854-5635, USA.
SOURCE: RNA (New York, N.Y.), (1997 Aug) 3 (8) 870-81. Journal code: 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970922
Last Updated on STN: 20000303
Entered Medline: 19970905
AB The translation elongation feactor 1alpha (EF-1alpha) catalyzes the critical step of delivering aminoacyl-tRNAs to the elongating ribosome. A series of Saccharomyces cerevisiae strains containing mutant alleles of the TEF2 gene encoding EF-1alpha have phenotypes consistent with effects on cellular processes related to translation. These include (1) conditional growth defects, (2) antibiotic sensitivity or resistance, (3) altered +1 or -1 **ribosomal** frameshifting efficiencies, and (4) altered maintenance of the killer phenotype. Although all the mutant alleles were isolated as dominant +1 **frameshift** suppressors, the effects of these mutations on the cell are quite different when present as the only form of EF-1alpha. Allele-specific effects are observed with regard to their ability to alter the efficiency of programmed +1 frameshifting as opposed to programmed -1 **ribosomal** frameshifting. The significantly altered efficiency of -1 frameshifting in strains containing the TEF2-4 and TEF2-9 mutant alleles further correlates with a reduced ability to maintain the killer phenotype and the M1 satellite virus of L-A, an in vivo assay of translational fidelity. In light of the proposed models regarding the different A- and P-site

occupancy states required for +1 or -1 **ribosomal** frameshifting, these results aid analysis of interactions between EF-1alpha and the translational apparatus.

L7 ANSWER 21 OF 26 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 97051830 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8896465
TITLE: Mof4-1 is an allele of the UPF1/IFS2 gene which affects both mRNA turnover and -1 **ribosomal** frameshifting efficiency.
AUTHOR: Cui Y; **Dinman J D**; Peltz S W
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Cancer Institute of New Jersey, Piscataway 08854, USA.
CONTRACT NUMBER: AI07403-05 (NIAID)
GM48631-01 (NIGMS)
SOURCE: EMBO journal, (1996 Oct 15) 15 (20) 5726-36.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961206
AB The mof4-1 (maintenance of frame) allele in the yeast Saccharomyces cerevisiae was isolated as a chromosomal mutation that increased the efficiency of -1 **ribosomal** frameshifting at the L-A virus **frameshift** site and caused loss of M1, the satellite virus of L-A. Here, we demonstrate that strains harboring the mof4-1 allele inactivated the nonsense-mediated mRNA decay pathway. The MOF4 gene was shown to be allelic to UPF1, a gene whose product is involved in the nonsense-mediated mRNA decay pathway. Although cells harboring the mof4-1 allele of the UPF1 gene lose the M1 virus, mutations in other UPF genes involved in nonsense-mediated mRNA decay maintain the M1 virus. The mof4-1 strain is more sensitive to the aminoglycoside antibiotic paromomycin than a upf1 delta strain, and frameshifting efficiency increases in a mof4-1 strain grown in the presence of this drug. Further, the ifs1 and ifs2 alleles previously identified as mutations that enhance frameshifting were shown to be allelic to the UPF2 and UPF1 genes, respectively, and both ifs strains maintained M1. These results indicate that mof4-1 is a unique allele of the UPF1 gene and that the gene product of the mof4-1 allele affects both -1 **ribosomal** frameshifting and mRNA turnover.

L7 ANSWER 22 OF 26 MEDLINE on STN
ACCESSION NUMBER: 96042897 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8536994
TITLE: 5 S rRNA is involved in fidelity of translational reading frame.
AUTHOR: **Dinman J D**; Wickner R B
CORPORATE SOURCE: Section on Genetics of Simple Eukaryotes, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: Genetics, (1995 Sep) 141 (1) 95-105.
Journal code: 0374636. ISSN: 0016-6731.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199602
ENTRY DATE: Entered STN: 19960221
Last Updated on STN: 19960221
Entered Medline: 19960208
AB Chromosomal mutants (maintenance of frame = mof) in which the efficiency of -1 **ribosomal** frameshifting is increased can be isolated using constructs in which lacZ expression is dependent upon a -1 shift of

reading frame. We isolate a new mof mutation, mof9, in Saccharomyces cerevisiae and show that it is complemented by both single and multi-copy 5 S rDNA clones. Two independent insertion mutations in the rDNA locus (rDNA::LEU2 and rDNA::URA3) also display the Mof- phenotype and are also complemented by single and multi-copy 5 S rDNA clones. Mutant 5 S rRNAs expressed from a plasmid as 20-50% of total 5 S rRNA in a wild-type host also induced the Mof- phenotype. The increase in frameshifting is greatest when the lacZ reporter gene is expressed on a high copy, episomal vector. No differences were found in 5 S rRNA copy number or electrophoretic mobilities in mof9 strains. Both mof9 and rDNA::LEU2 increase the efficiency of +1 frameshifting as well but have no effect on readthrough of UAG or UAA termination codons, indicating that not all translational specificity is affected. These data suggest a role for 5 S rRNA in the maintenance of frame in translation.

L7 ANSWER 23 OF 26 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 95050293 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7961484
TITLE: SPE1 and SPE2: two essential genes in the biosynthesis of polyamines that modulate +1 **ribosomal** frameshifting in Saccharomyces cerevisiae.
AUTHOR: Balasundaram D; **Dinman J D**; Tabor C W; Tabor H
CORPORATE SOURCE: Laboratory of Biochemical Pharmacology, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Maryland 20892-0830.
SOURCE: Journal of bacteriology, (1994 Nov) 176 (22) 7126-8.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941216
AB We previously showed that a mutant of Saccharomyces cerevisiae, which cannot make spermidine as a result of a deletion in the SPE2 gene (spe2 delta), exhibits a marked elevation in +1 **ribosomal** frameshifting efficiency in response to the Ty1 **frameshift** sequence, CUU AGG C. In the present study, we found that spermidine deprivation alone does not result in increased +1 **ribosomal** frameshifting efficiency. The high level of +1 **ribosomal** frameshifting efficiency in spe2 delta cells is the result of the combined effects of both spermidine deprivation and the large increase in the level of intracellular putrescine resulting from the derepression of the gene for ornithine decarboxylase (SPE1) in spermidine-deficient strains.

L7 ANSWER 24 OF 26 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 94186067 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8138178
TITLE: Translational maintenance of frame: mutants of Saccharomyces cerevisiae with altered -1 **ribosomal** frameshifting efficiencies.
AUTHOR: **Dinman J D**; Wickner R B
CORPORATE SOURCE: Laboratory of Biochemical Pharmacology, National Institute of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland 20892.
SOURCE: Genetics, (1994 Jan) 136 (1) 75-86.
Journal code: 0374636. ISSN: 0016-6731.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940509
Last Updated on STN: 19940509
Entered Medline: 19940425
AB A special site on the (+) strand of the L-A dsRNA virus induces about 2% of ribosomes translating the gag open reading frame to execute a -1

frameshift and thus produce the viral gag-pol fusion protein. Using constructs in which a -1 **ribosomal frameshift** at this site was necessary for expression of lacZ we isolated chromosomal mutants in which the efficiency of frameshifting was increased. These mutants comprise eight genes, named mof (maintenance of frame). The mof1-1, mof2-1, mof4-1, mof5-1 and mof6-1 strains cannot maintain M1 dsRNA at 30 degrees, but, paradoxically, do not lose L-A. The mof2-1, mof5-1 and mof6-1 strains are temperature sensitive for growth at 37 degrees, and all three show striking cell cycle phenotypes. The mof2-1 strains arrest with mother and daughter cells almost equal in size, mof5-1 arrests with multiple buds and mof6-1 arrests as single large unbudded cells. mof2-1 and mof5-1 strains are also Pet-. The mof mutations show differential effects on various frameshifting signals.

L7 ANSWER 25 OF 26 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 92260639 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1583726
TITLE: **Ribosomal** frameshifting efficiency and gag/gag-pol ratio are critical for yeast M1 double-stranded RNA virus propagation.
AUTHOR: **Dinman J D**; Wickner R B
CORPORATE SOURCE: Section on the Genetics of Simple Eukaryotes, National Institute of Diabetes, Digestive and Kidney Diseases, Bethesda, Maryland 20892.
SOURCE: Journal of virology, (1992 Jun) 66 (6) 3669-76. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 19920626
Last Updated on STN: 19920626
Entered Medline: 19920616

AB About 1.9% of ribosomes translating the gag open reading frame of the yeast L-A double-stranded RNA virus positive strand undergo a -1 **frameshift** and continue translating in the pol open reading frame to make a 170-kDa gag-pol fusion protein. The importance of frameshifting efficiency for viral propagation was tested in a system where the M1 (killer toxin-encoding) satellite RNA is supported by a full-length L-A cDNA clone. Either increasing or decreasing the **frameshift** efficiency more than twofold by alterations in the slippery site disrupted viral propagation. A threefold increase caused by a chromosomal mutation, hsh1 (high shifter), had the same effect. Substituting a +1 **ribosomal frameshift** site from Ty1 with the correct efficiency also allowed support of M1 propagation. The normal -1 **frameshift** efficiency is similar to the observed molar ratio in viral particles of the 170-kDa gag-pol protein to the 70-kDa gag gene product, the major coat protein. The results are interpreted in terms of a packaging model for L-A.

L7 ANSWER 26 OF 26 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 91095422 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1986362
TITLE: A -1 **ribosomal frameshift** in a double-stranded RNA virus of yeast forms a gag-pol fusion protein.
AUTHOR: **Dinman J D**; Icho T; Wickner R B
CORPORATE SOURCE: Section on the Genetics of Simple Eukaryotes, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1991 Jan 1) 88 (1) 174-8. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102

ENTRY DATE: Entered STN: 19910322
Last Updated on STN: 19910322
Entered Medline: 19910214

AB The L-A double-stranded RNA (dsRNA) virus of Saccharomyces cerevisiae has two open reading frames (ORFs). ORF1 encodes the 80-kDa major coat protein (gag). ORF2, which is expressed only as a 180-kDa fusion protein with ORF1, encodes a single-stranded RNA-binding domain and has the consensus sequence for RNA-dependent RNA polymerases of (+)-strand and double-stranded RNA viruses (pol). We show that the 180-kDa protein is formed by -1 **ribosomal** frame-shifting by a mechanism indistinguishable from that of retro-viruses. Analysis of the "slippery site" suggests that a low probability of unpairing of the aminoacyl-tRNA from the 0-frame codon at the **ribosomal** A site reduces the efficiency of frameshifting more than the reluctance of a given tRNA to have its wobble base mispaired. Frameshifting of L-A requires a pseudoknot structure just downstream of the shift site. The efficiency of the L-A **frameshift** site is 1.8%, similar to the observed molar ratio in viral particles of the 180-kDa fusion protein to the major coat protein.

L10 ANSWER 1 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:281522 BIOSIS
DOCUMENT NUMBER: PREV199900281522
TITLE: Identification of putative programmed -1 **ribosomal frameshift** signals in large DNA databases.
AUTHOR(S): Hammell, Amy B.; Taylor, Ronald C.; **Peltz, Stuart W.**; Dinman, Jonathan D. [Reprint author]
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Robert Wood Johnson Medical School, Graduate Programs in Molecular Bioscience Rutgers/UMDNJ, University of Medicine and Dentistry of New Jersey (UMDNJ), Piscataway, NJ, 08854, USA
SOURCE: Genome Research, (May, 1999) Vol. 9, No. 5, pp. 417-427. print.
ISSN: 1088-9051.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jul 1999
Last Updated on STN: 28 Jul 1999

AB The cis-acting elements that promote efficient ribosomal frameshifting in the -1 (5') direction have been well characterized in several viral systems. Results from many studies have convincingly demonstrated that the basic molecular mechanisms governing programmed -1 ribosomal frameshifting are almost identical from yeast to humans. We are interested in testing the hypothesis that programmed -1 ribosomal frameshifting can be used to control cellular gene expression. Toward this end, a computer program was designed to search large DNA databases for consensus -1 **ribosomal frameshift** signals. The results demonstrated that consensus programmed -1 **ribosomal frameshift** signals can be identified in a substantial number of chromosomally encoded mRNAs and that they occur with frequencies from two- to sixfold greater than random in all of the databases searched. A preliminary survey of the databases resulting from the computer searches found that consensus frameshift signals are present in at least 21 homologous genes from different species, 2 of which are nearly identical, suggesting evolutionary conservation of function. We show that four previously described missense alleles of genes that are linked to human **diseases** would disrupt putative programmed -1 **ribosomal frameshift** signals, suggesting that the frameshift signal may be involved in the normal expression of these genes. We also demonstrate that signals found in the yeast RAS1 and the human CCR5 genes were able to promote significant levels of programmed -1 ribosomal frameshifting. The significance of these frameshifting signals in controlling gene expression is not known, however.

L12 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:191205 CAPLUS
DOCUMENT NUMBER: 132:233328
TITLE: **Ribosomal frameshift** target identification and used for regulating gene expression
INVENTOR(S): Dinman, Jonathan D.; **Peltz, Stuart W.**
PATENT ASSIGNEE(S): University of Medicine and Dentistry, USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015782	A1	20000323	WO 1999-US20942	19990913
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9959199	A1	20000403	AU 1999-59199	19990913
PRIORITY APPLN. INFO.:			US 1998-100285P P	19980914
			WO 1999-US20942 W	19990913

AB Sequences involved in ribosomal frameshifting have been discovered in mammalian genes. A computer search was designed to search for consensus -1 **ribosomal frameshift** signals (motif hits) present in the EMBL virus, Saccharomyces cerevisiae, human mRNA, cDNA, and Expressed Sequence Tag databases. These searches found that potential -1 ribosomal frameshifting signals occur at frequencies greater than one order of magnitude above random chance. This result provides strong theor. evidence for the existence of a subset of cellular genes which are regulated at the translational level by -1 ribosomal frameshifting in eukaryotes, and that this post-transcriptional regulatory mechanism is widely used by many different families of viruses as well. The present invention provides a method of identifying a nucleic acid sequence involved in ribosomal frameshifting. The method comprises (1) searching a database of gene sequences to identify sequences which contain the sequence XXXYYYZ, wherein XXX represents GGG, AAA, TTT, or CCC; YYY represents AAA or TTT; Z represents A, T, or C; and wherein XXXYYYZ is not AAAAAAA or TTTTTTT; and (2) further searching among those sequences identified in step 1 for a sequence encoding a pseudoknot structure which is within 8 nucleotides of the sequence identified in step 1. Methods of regulating gene expression by modulating ribosomal frameshifting are disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 1999:281522 BIOSIS
DOCUMENT NUMBER: PREV199900281522
TITLE: Identification of putative programmed -1 **ribosomal frameshift** signals in large DNA databases.
AUTHOR(S): Hammell, Amy B.; Taylor, Ronald C.; **Peltz, Stuart W.**; Dinman, Jonathan D. [Reprint author]
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Robert Wood Johnson Medical School, Graduate Programs in Molecular Bioscience Rutgers/UMDNJ, University of Medicine and Dentistry of New Jersey (UMDNJ), Piscataway, NJ, 08854, USA
SOURCE: Genome Research, (May, 1999) Vol. 9, No. 5, pp. 417-427. print.
ISSN: 1088-9051.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Jul 1999
Last Updated on STN: 28 Jul 1999

AB The cis-acting elements that promote efficient ribosomal frameshifting in the -1 (5') direction have been well characterized in several viral systems. Results from many studies have convincingly demonstrated that the basic molecular mechanisms governing programmed -1 ribosomal frameshifting are almost identical from yeast to humans. We are interested in testing the hypothesis that programmed -1 ribosomal frameshifting can be used to control cellular gene expression. Toward this end, a computer program was designed to search large DNA databases for consensus -1 **ribosomal frameshift** signals. The results demonstrated that consensus programmed -1 **ribosomal frameshift** signals can be identified in a substantial number of chromosomally encoded mRNAs and that they occur with frequencies from two- to sixfold greater than random in all of the databases searched. A preliminary survey of the databases resulting from the computer searches found that consensus frameshift signals are present in at least 21 homologous genes from different species, 2 of which are nearly identical, suggesting evolutionary conservation of function. We show that four previously described missense alleles of genes that are linked to human diseases would disrupt putative programmed -1 **ribosomal frameshift** signals, suggesting that the frameshift signal may be involved in the normal expression of these genes. We also demonstrate that signals found in the yeast RAS1 and the human CCR5 genes were able to promote significant levels of programmed -1 ribosomal frameshifting. The significance of these frameshifting signals in controlling gene expression is not known, however.

L12 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 2
ACCESSION NUMBER: 1999:73926 BIOSIS
DOCUMENT NUMBER: PREV199900073926
TITLE: Ribosomal protein L3 mutants alter translational fidelity and promote rapid loss of the yeast killer virus.
AUTHOR(S): **Peltz, Stuart W.**; Hammell, Amy B.; Cui, Ying; Yasenchak, Jason; Puljanowski, Lara; Dinman, Jonathan D. [Reprint author]
CORPORATE SOURCE: Dep. Molecular Genetics Microbiol. Graduate Program Molecular Biosciences UMDNJ/Rutgers Universities, 675 Hoes Lane, Piscataway, NJ 08854, USA
SOURCE: Molecular and Cellular Biology, (Jan., 1999) Vol. 19, No. 1, pp. 384-391. print.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999

AB Programmed -1 ribosomal frameshifting is utilized by a number of RNA viruses as a means of ensuring the correct ratio of viral structural to enzymatic proteins available for viral particle assembly. Altering frameshifting efficiencies upsets this ratio, interfering with virus propagation. We have previously demonstrated that compounds that alter the kinetics of the peptidyl-transfer reaction affect programmed -1 **ribosomal frameshift** efficiencies and interfere with viral propagation in yeast. Here, the use of a genetic approach lends further support to the hypothesis that alterations affecting the ribosome's peptidyltransferase activity lead to changes in frameshifting efficiency and virus loss. Mutations in the RPL3 gene, which encodes a ribosomal protein located at the peptidyltransferase center, promote approximately three- to fourfold increases in programmed - 1 **ribosomal frameshift** efficiencies and loss of the M1 killer virus of yeast. The mak8-1 allele of RPL3 contains two adjacent missense mutations which are predicted to structurally alter the Mak8-1p. Furthermore, a second allele that encodes the N-terminal 100 amino acids of L3 (called L3A) exerts a trans-dominant effect on programmed -1 ribosomal frameshifting and killer virus maintenance. Taken together, these results support the hypothesis that alterations in the

peptidyltransferase center affect programmed -1 ribosomal frameshifting.

L12 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 3
ACCESSION NUMBER: 1998:361753 BIOSIS
DOCUMENT NUMBER: PREV199800361753
TITLE: The Upf3 protein is a component of the surveillance complex that monitors both translation and mRNA turnover and affects viral propagation.
AUTHOR(S): Ruiz-Echevarria, Maria J.; Yasenchak, Jason M.; Han, Xia; Dinman, Jonathan D.; **Peltz, Stuart W.** [Reprint author]
CORPORATE SOURCE: Dep. Molecular Genetics Microbiol., Univ. Med. Dentistry New Jersey/Rutgers Univ., New Brunswick, NJ, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (July 21, 1998) Vol. 95, No. 15, pp. 8721-8726. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 1998
Last Updated on STN: 27 Aug 1998

AB The nonsense-mediated mRNA decay pathway functions to degrade aberrant mRNAs that contain premature translation termination codons. In Saccharomyces cerevisiae, the Upf1, Upf2, and Upf3 proteins have been identified as trans-acting factors involved in this pathway. Recent results have demonstrated that the Upf proteins may also be involved in maintaining the fidelity of several aspects of the translation process. Certain mutations in the UPF1 gene have been shown to affect the efficiency of translation termination at nonsense codons and/or the process of programmed -1 ribosomal frameshifting used by viruses to control their gene expression. Alteration of programmed frameshift efficiencies can affect virus assembly leading to reduced viral titers or elimination of the virus. Here we present evidence that the Upf3 protein also functions to regulate programmed -1 frameshift efficiency. A upf3-DELTA strain demonstrates increased sensitivity to the antibiotic paromomycin and increased programmed -1 **ribosomal frameshift** efficiency resulting in loss of the-M1 virus. Based on these observations, we hypothesize that the Upf proteins are part of a surveillance complex that functions to monitor translational fidelity and mRNA turnover.

L12 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:324475 CAPLUS
DOCUMENT NUMBER: 126:297658
TITLE: Proteins involved in targeting of peptidyl transfer center, and corresponding therapeutic agents and methods
INVENTOR(S): **Peltz, Stuart W.**; Dinman, Jonathan D.; Cui, Ying
PATENT ASSIGNEE(S): University of Medicine and Dentistry, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9712617	A1	19970410	WO 1996-US16011	19961004
W: AU, CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2234229	AA	19970410	CA 1996-2234229	19961004
AU 9675149	A1	19970428	AU 1996-75149	19961004
AU 730902	B2	20010315		
EP 854722	A1	19980729	EP 1996-937660	19961004
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

JP 2002515855 T2 20020528 JP 1997-514502 19961004
PRIORITY APPLN. INFO.: US 1995-5041P P 19951006
WO 1996-US16011 W 19961004

AB MRNA degradation is an important control point in the regulation of gene expression and has been shown to be linked to the process of translation. One clear example of this linkage is the observation that nonsense mutations accelerate the degradation of mRNAs. In this report we demonstrate that a subset of the mof alleles (maintenance of frame) in yeast, which were isolated as chromosomal mutations that increased the frameshifting efficiency at the L-A virus frameshift site and caused loss of the L-A satellite virus M1, also affect the nonsense-mediated mRNA decay pathway. The levels of nonsense-containing mRNAs were elevated in cells harboring the mof4-1 alleles. Furthermore, mof4-1 is allelic to UPF1, which has been demonstrated to be involved in the nonsense-mediated mRNA decay pathway. Although cells harboring the mof4-1 allele lose the M1 virus, the other f alleles (i.e., upf1, upf2 and upf3) involved in nonsense-mediated mRNA decay maintain M1. The ifs1 and ifs2 alleles previously identified as mutations that enhance frameshifting at the -1 **ribosomal frameshift** signal from the mouse mammary tumor virus were shown to be allelic to the UPF2 and UPF1 genes, resp., and both ifs strains maintained M1. The mof4-1 strain is more sensitive to the aminoglycoside paromomycin than a upf1$g(D) strain, and frameshifting efficiency increases in a mof4-1 strain grown in the presence of paromomycin, These results indicate that the upf1p has a dual function in both translation and mRNA turnover.

L12 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 1997:341645 BIOSIS
DOCUMENT NUMBER: PREV199799640848
TITLE: Peptidyl-transferase inhibitors have antiviral properties by altering programmed -1 ribosomal frameshifting efficiencies: Development of model systems.
AUTHOR(S): Dinman, Jonathan D. [Reprint author]; Ruiz-Echevarria, Maria J.; Czaplinski, Kevin; **Peltz, Stuart W.**
CORPORATE SOURCE: Dep. Molecular Genetics Microbiol., Univ. Med. Dentistry New Jersey, Robert Wood Johnson Med. Sch., Graduate Programs Molecular Bioscience, 675 Hoes Lane, Piscataway, NJ 08854, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 13, pp. 6606-6611.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Aug 1997
Last Updated on STN: 11 Aug 1997

AB The effects of two peptidyl-transferase inhibitors, anisomycin and sparsomycin, on ribosomal frameshifting efficiencies and the propagation of yeast double-stranded RNA viruses were examined. At sublethal doses in yeast cells these drugs specifically alter the efficiency of - 1, but not of + 1, ribosomal frameshifting. These compounds promote loss of the yeast L-A double-stranded RNA virus, which uses a programmed -1 **ribosomal frameshift** to produce its Gag-Pol fusion protein. Both of these drugs also change the efficiency of -1 ribosomal frameshifting in yeast and mammalian in vitro translation systems, suggesting that they may have applications to control the propagation of viruses of higher eukaryotes, which also use this translational regulatory mechanism. Our results offer a new set of antiviral agents that may potentially have a broad range of applications in the clinical, veterinary, and agricultural fields.

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